OPEN ACCESS

ORIGINAL ARTICLE

Evaluating the frequency of antibiotic consumption in a PICU of a tertiary care hospital in Karachi: A Prospective study

Rubab Naz, Hanif Kamal, Anwar Ul Haque, Safa Alam, Atika Sher, Muhammad Irfan

Liaquat National Hospital and Medical College, Karachi Pakistan

ABSTRACT

Background: Antibiotics have transformed the medical field; however, the increase in antimicrobial resistance (AMR) threatens their effectiveness, particularly in Pediatric Intensive Care Units (PICUs), where critically ill children are highly vulnerable to infections. This study aimed to analyze the antibiotic utilization trends in a tertiary care PICU in Pakistan to improve antibiotic stewardship.

Material and Methods: A prospective observational study was conducted in the PICU of a tertiary-care hospital in Karachi, Pakistan, from 1st June 2023 to 31st May 2024. All critically ill children (1 month to 15 years) admitted in the PICU, regardless of the antibiotic exposure were included, excluding immunocompromised children or those who were discharged before 72 hours. Antibiotics were categorized as empirical, therapeutic, or prophylactic. Empirical antibiotics outcomes after 72 hours were classified as "remains unchanged," "discontinued," "changed," or "continued as therapeutics".

Results: Of 265 admissions, 257 (97%) received antibiotics, predominantly Empirical (89.1%). On the first day, 59.1% received monotherapy, primarily Ceftriaxone (57.9%); whereas 39.3% received dual-therapy, most often Meropenem-Vancomycin (37.6%). After 72 hours, empirical therapy remained unchanged in 63% of cases, changed in 15.6%, discontinued in 16.2%, and continued as therapeutic in 5.2%. The median duration of antibiotic therapy was 5 days (IQR: 4-8). The total multidrug-resistance organism (MDRO) rate was 7.6% and mortality rate was 6.6%.

Conclusion: Antibiotics use in the PICU was extensive and predominantly empirical, with limited reassessment after initiation. These findings highlight the importance to strengthen antimicrobial stewardship practices, optimize antibiotic utilization, and mitigate the emergence of AMR in PICU.

Keywords: Antibiotic Stewardship, Empirical Therapy, LMICs, PICU.

BACKGROUND

Antibiotics are crucial in treating life-threatening infections and preventing hospital acquired infections (HAIs), yet their misuse can cause significant disadvantages, including antibiotic resistance, adverse drug events, increased morbidity, and higher healthcare costs.[1] Children admitted to Pediatric Intensive Care Units (PICUs) are particularly vulnerable to infections because of critical illness, invasive device use and prolonged hospitalization. Consequently, they are at increased risk of acquiring HAIs, which has been reported in 4.7%-20.2% of PICU cases.[2-4] As a consequence, antibiotic utilization is more frequent in PICU settings, ranges from 50-100%, as have been reported in previous studies.[3-8] It has also become a norm to prescribe antibiotics to almost all admission in PICU regardless of the absence of any infectious sign.[5] Additionally, children often receive broad-spectrum antibiotics, although narrow-spectrum antibiotics may be adequate.[9] Another study found that 30–50% of antibiotics used were deemed inappropriate, with half of these antibiotics considered unnecessary.[2,3] A study conducted in Karachi in 2016 reported that antibiotic use In a PICU was 42% empirical, 43% prophylactic, and 15% therapeutic.[7] while a study conducted in Riyadh in 2020 reported these uses as 68.2%, 22.3%, and 9.5%, respectively.[3] These differences likely reflect local demographics, hygiene, economic conditions, prescribing habits and local antibiotic resistance.

A recent study from New Delhi, India, reported increasing resistance among common bacterial pathogens to third-generation Cephalosporins (4-100%) and Meropenem (27.8%-57%),[8] highlighting the

Correspondence: Dr. Rubab Naz, Pediatrics Medicine Trainee, Liaquat National Hospital, Karachi Pakistan

Email: rubabnaz1@gmail.com

This article can be cited as: Naz R, Kamal H, Haque AU, Alam S, Sher A, Irfan M. Evaluating the frequency of antibiotic consumption in a PICU of a tertiary care hospital in Karachi: A Prospective study. Infect Dis J Pak. 2026; 35(2): 117-125.

DOI: https://doi.org/10.61529/idjp.v35i2.430

Receiving date: **16 Jul 2025** Acceptance Date: **19 Jun 2026**
Revision date: **02 Apr 2026** Publication Date: **30 Jun 2026**

growing burden of AMR in pediatric critical care settings.

In 2015, the World Health Organization (WHO) launched a comprehensive global strategy to combat AMR.[10] Antibiotics stewardship programs (ASP) are advised to reduce the inappropriate antibiotic use[11] but this mandates an understanding of the local patterns of antibiotic use and rationale. Although, there are many studies on antibiotic use in PICU from developed countries, there remains a major knowledge gap in PICUs of developing nations, like in Pakistan. With the evolving resistance patterns, our study aims to evaluate antibiotic utilization patterns in a tertiary-care PICU through prospective medical record reviews, and identify areas of strengthening antimicrobial stewardship practices.

MATERIAL AND METHODS

This descriptive prospective observational study was conducted in a Pakistani tertiary-care PICU from 1st June 2023 to 31st May 2024 (IRB/ ERC letter number App # 0900-2023-LNH-ERC dated May 31st 2023. All children aged 1 month to 15 years admitted in our PICU for >72 hours, regardless of the antibiotic exposure were included. Exclusion criteria were: age <1 month or >15 years, discharge before 72 hours (as microbiological cultural and sensitivity results generally require approximately 72 hours to become available, limiting the ability to evaluate subsequent antibiotic-related decisions), immunocompromised status, or oncologic diseases. Only antibiotics administered during the PICU stay were included; treatments before or after the PICU admission were excluded.

Sample size was calculated by WHO sample size calculator assuming prevalence of antibiotics use among children admitted in PICU as 80%,[12] margin of error as 5% and 95% confidence interval, yielding 246 patients. After adding contingency of 8% for missing and incomplete data, the final sample size was 265. Patient’s medical records were scrutinized daily. Consecutive patients entering the PICU, irrespective of their prior admission history, were included in the study, with PCU admission day was designated as day-1 of the study. Demographic details, clinical diagnosis, details of antibiotic use (type of antibiotic, name and length of treatment, change in the antibiotic regimen, total number of drugs prescribed, fate of empirical antibiotics), culture and sensitivity data and length of stay were recorded in an online Google spreadsheet. Antibiotic resistance data for all samples isolated during the period of study were also assessed. We followed STROBE guidelines.

For empirical antibiotic therapy, outcomes after 72 hours were categorized as discontinued, changed (based on microbiological results and/or clinical condition), remained unchanged (as there was no documented decision, resulting in continuation of the same antibiotics), and continued as therapeutic (when culture results demonstrated the same susceptibility). Days of Therapy (DOT) was defined as the total number of days a patient received each antibiotic agent, regardless of dosage. If a patient received more than one antibiotic simultaneously, each individual antibiotic received per day represents 1 DOT. Contaminants are defined as microorganisms isolated from cultures that were considered unlikely to present true infection bases on their clinical and microbiological findings. These typically included organisms commonly recognized as skin or environmental flora and isolated in the absence of clinical, laboratory, or microbiological evidence supporting infection. The MDRO rate was defined as the proportion of patients with at least one multidrug-resistant organism isolated during hospitalization, with repeated isolates from the same patient counted as one. Similarly, the HAI rate represented the proportion of patients who developed at least one hospital-acquired infection, irrespective of the number of episodes.

Data analysis was performed using SPSS version 27. Quantitative variables were presented as mean ± standard deviations or median with interquartile range, while qualitative variables were presented as frequencies and percentages. chi-square/fisher exact tests were applied to determine association between qualitative variables. p-value ≤0.05 were considered statistically significant.

Ethical approval was obtained from the hospitals Ethical Research Committee (ERC # 0900-2023-LNH-ERC). Patients' confidentiality was maintained and informed consent was waived because the study involved the review of patient charts and laboratory reports only.

RESULTS

Of 265 children, 97% (257/265) received antibiotics. Further study analysis included only antibiotics recipients. Antibiotic recipients had a median age of 1.5 years (IQR: 0.5-6.0 years) and a higher proportion were of males (63.4%). Comorbidities were observed in 33.5% of patients. Medical conditions constituted the main cause for admission (89.5%), with respiratory illnesses being the most common (43.0%) (Table-I).

The study accounted for 1,304 patient-days and 1,958 Days Of antibiotic Therapy (DOT), corresponding to approximately 1.5 antibiotic days/ patient. Antibiotic utilization was predominantly empirical (89.1%; 229/257), while prophylactic and therapeutic use were 10.1% (26/257) and 0.8% (2/257), respectively. Median number of antibiotics given to the children, throughout their stay in the PICU, were 2 (IQR: 1-2).

Day-1 antibiotics: On admission, 59.1% (152) received monotherapy, predominantly Ceftriaxone (57.9%; 88/152), followed by Piperacilin-tazobactam (25.7%; 38/152) and Meropenem (7.2%; 11/152). Dual therapy rate was 39.3% (101), most commonly Meropenem-Vancomycin (37.6%; 38/101), followed by Ceftriaxone-Vancomycin (19.8%; 20/101) and Cefotaxime-Amikacin (9.9%; 10/101). Triple therapy rate was 1.6% (4), predominantly Meropenem-Vancomycin-Colistin.

Throughout hospitalization antibiotics: During the hospital stay, 42.4% were prescribed one antibiotic, 35% were prescribed two, 14.4% were given three, and 8.2% received more than three antibiotics. Ceftriaxone was the top prescribed antibiotic overall (48.6%), followed by meropenem (33.9%), vancomycin (33.9%), and piperacillin-tazobactam (27.6%).

After 72 hours, empirical antibiotic therapy remained unchanged in 63.0% of patients, whereas treatment was changed in 15.6%, discontinued in 16.2% and continued as therapeutic in 5.2%. Median duration of antibiotic use was 5 days (IQR: 4-8). Most patients (66.9%) were given antibiotics for less than 7 days. While 19.1% received antibiotics for 8–14 days, and 14%for >15 days. Prophylactic antibiotics mainly included ceftriaxone (63.0%) or vancomycin (37.0%) separately, or combinations of ceftriaxone-vancomycin (50.0%) and meropenem-vancomycin (30.8%).

Age- stratified analysis revealed greater use of amikacin (86.7%, $p = 0.001$) and cefotaxime (94.7%, $p < 0.001$) in infants and piperacillin-tazobactam in children under five years (86.0%, $p = 0.017$), without significant age-based differences in other antibiotics and outcomes (Table-II).

Among the 257 children who received antibiotics, cultures were sent for only 237 children during their hospitalization.

Day-1 cultures: Out of 237 children, 258 culture samples were sent from 228 children (228/237 = 96.2%) on day-1 of admission, showing an overall positivity rate of 26% (67/258). Among 216 blood culture samples, only 7.9% (17/216) showed growth of pathogens and 18.5% (40/216) were contaminants.

Most common isolates on Day-1 culture: *XDR* (Extensively Drug-Resistant) *Salmonella Typhi* (27.8%) was the most common pathogen in blood samples, whereas *Methicillin-resistant Staphylococcus aureus* (MRSA) predominates in non-blood samples (20%). *Vibrio cholera* represented 43.5% of isolates from stool samples.

Overall Cultures during hospitalization: During hospitalization, 434 samples were sent for culture from 257 patients. The overall positivity rate was 26.5% (115/434). Blood culture which constituted the majority of samples, demonstrated a low pathogen yield 10.6% (31/292) with a high contamination rate 16.8% (49/292). Whereas, no contamination was observed in non-blood specimens. Positivity rates were highest in other (non-blood) specimens, including, pus, wound, pleural and peritoneal fluid (46.7%; 7/15), stool (46.2%; 6/13), tracheal aspirates (44.4%; 8/18), followed by urine (20.7%; 12/58) and cerebrospinal fluid cultures (5.3%; 2/38).

Th most common bloodstream isolate was *XDR Salmonella Typhi*, *followed* by *Stenotrophomonas maltophilia*, *MDR* (multidrug resistant) *Acinetobacter*, *MRSA*, *Enterococcus species* and *Candida albicans*.

Resistance patterns: Analysis of the antimicrobial resistance patterns according to CLSI criteria, indicated that ESBL (Extended-spectrum Beta-lactamase) -producing *Escherichia coli* exhibited 100% resistance to third-generation Cephalosporins and Piperacillin-Tazobactam while showing 100% sensitivity to Carbapenems. Likewise, *XDR Salmonella Typhi* also showed 100% resistance to third-generation cephalosporin. Carbapenem resistance among the *MDR Acinetobacter isolates* was found to be at 75%, while 50% of *Enterococcus* isolates were resistant to Penicillin.

The overall prevalence of MDR pathogens was 7.6%. This burden was predominantly included MDR *Acinetobacter species*, *XDR Salmonella Typhi* and *ESBL*-producing organisms.

Clinical outcomes including HAIs, multi-organ dysfunction syndrome (MODS) and mortality were observed in 5.7%, 16% and 6.6% cases, respectively. The median hospital stay was 4 days (IQR: 3–6 days). Significant association was found between the number of antibiotics used and clinical outcomes. A higher proportion of patients receiving antibiotics for ≥3 days had prolonged hospitalization (>7 days; 41.4% vs 7.0%), higher rates of severe complications (MODS: 43.1% vs 8.0%; HAI: 17.2% vs 2.5%), and greater mortality (19.0% vs 3.0%), compared with those treated for <3 days. (Table-III).

Among 257 patients, 33.1% (85) received antibiotics for >7 days. Regression analysis revealed invasive devise to be independently associated with prolonged therapy (aOR: 2.46, p=0.049), while use of<3 antibiotics were significantly protective against prolonged therapy (aOR: 0.078, p<0.001) (Figure-1a). For HAIs, invasive device use (aOR: 3.76, p=0.046) and MODS (aOR: 10.38, p=0.002) were significant predictors. (Figure-1b)

Table-I: Sociodemographic and clinical characteristics of children admitted in pediatric intensive care unit prescribed at least one antibiotic (n=257).

	n (%)
Age (years); median (Q1-Q3)	1.50 (0.50 – 6.00)
Gender; Male	163(63.4)
Co-morbidity	86(33.5)
Invasive devices	41(16)
Admission Type	
Medical	230 (89.5)
System Involved (n=230)	
CNS	39(17)
Respiratory	99(43)
GIT	26(11.3)
CVS	6(2.6)
Multisystem	52(22.6)
Hematology	2(0.9)
Other	6(2.6)
Surgical	11 (4.3)
Trauma	16 (6.2)
Hospital Acquired Infection	15 (5.7)
Multi-organ dysfunction Syndrome (MODS)	41 (16)
Mortality	17 (6.6)
Duration of antibiotic use; median (Q1-Q3)	5 days (4-8)
Length of hospital stay; median (Q1-Q3)	4.00 (3.00 – 6.00)

Table-II: Antibiotic utilization patterns and clinical outcomes by age group.

Variable	**n (%)**			**p-value**
	<1 year (n=102)	**1-5 years (n=87)**	**>5 years (n=68)**	
Number of antibiotics				
<3	75 (37.7)	67 (33.7)	57 (28.6)	0.276
≥3	27 (46.6)	20 (34.5)	11 (19.0)	
Most common Antibiotic Agents				
Amikacin	13 (86.7)	1 (6.7)	1 (6.7)	**0.001***
Cefotaxime	18 (94.7)	0 (0)	1 (5.3)	**<0.001***
Piperacillin-Tazobactam	31 (43.7)	30 (42.3)	10 (14.1)	**0.017***
Meropenem	33 (37.9)	30 (34.5)	24 (27.6)	0.917
Vancomycin	36 (41.4)	26 (29.9)	25 (28.7)	0.618
Ceftriaxone	44 (35.2)	46 (36.8)	35 (28.0)	0.354
Colistin	11 (47.8)	10 (43.5)	2 (8.7)	0.127
Linezolid	4 (22.2)	8 (44.4)	6 (33.3)	0.288
Clinical Outcomes				
MODS				

Yes	17(41.5)	13(31.7)	11(26.8)	0.948
No	85(39.4)	74(34.3)	57(26.4)	
Mortality				
Yes	9 (52.9)	4 (23.5)	4 (23.5)	0.510
No	93(38.8)	83(34.6)	64(26.7)	
Hospital Stay (days)				
≤3	33(33.7)	31(31.6)	34(34.7)	0.116
4-7	53(43.8)	45(37.2)	23(19)	
>7	16(42.1)	11(28.9)	11(28.9)	

Chi-Square/fisher exact test was applied, P-value≤0.05 considered as Significant, *Significant at 0.05 levels, percentages represent row percentages unless specified otherwise

Table-III: Association of number of antibiotics with hospital stay, morbidity, mortality and hospital acquired infection.

	Number of antibiotics n (%)		p-value
	<3 (n=199)	≥3 (n=58)	
Hospital Stay			
≤3 days	89(44.7)	9(15.5)	<0.001*
4-7 days	96(48.2)	25(43.1)	
>7 days	14(7)	24(41.4)	
MODS			
Yes	16(8)	25(43.1)	<0.001*
No	183(92)	33(56.9)	
Mortality			
Yes	6(3)	11(19)	<0.001*
No	193(97)	47(81)	
Hospital acquired infection (HAI)			
Yes	5(2.5)	10(17.2)	<0.001*
No	194(97.5)	48(82.8)	

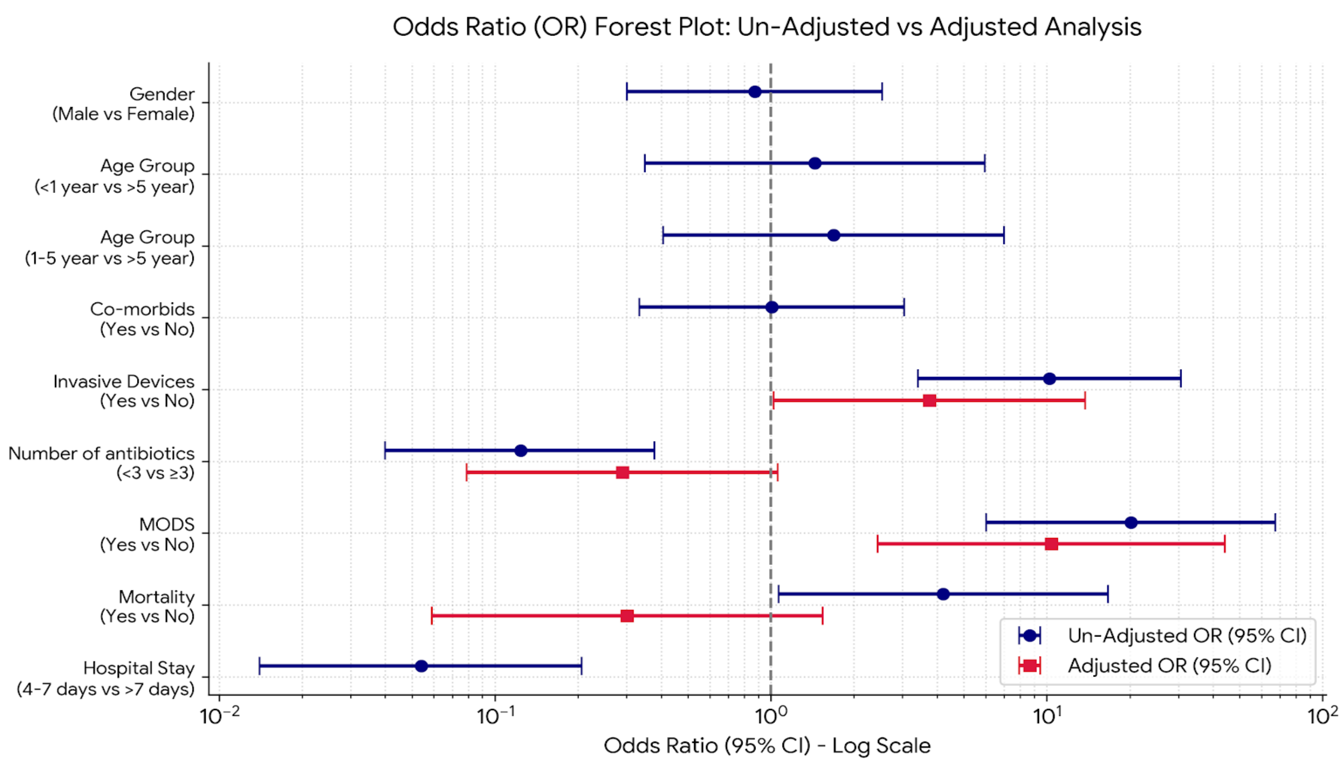

Figure-Ia: Forest Plot for binary regression analysis of factors associated with prolonged antibiotic use (> 7 days).

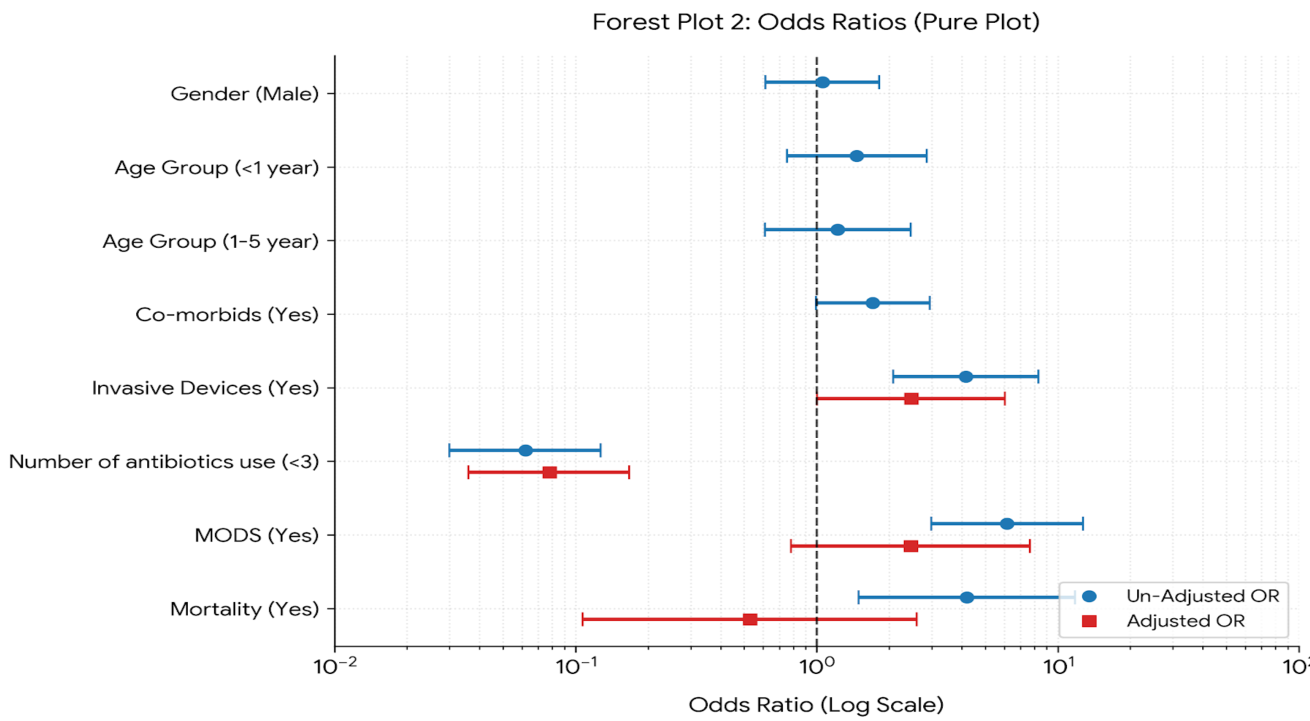

Figure-Ib: Forest Plot for binary regression analysis of factors associated with hospital acquired infections

DISCUSSION

The antibiotic utilization rate observed in the study was substantially higher than the WHO benchmarks of 20%-26.8%[8] and reports from Saudi Arabia (18.5%).[13] However, similar findings were reported from Italy (74.2%),[11] India (79.4% and 59.96%)[14,15] and Pakistan (100%)[7], suggesting that extensive antibiotic exposure remains common in critically ill children, particularly in low- and middle-income countries where critically ill children often require prompt empirical treatment.

The frequency of empirical antibiotic use in our study is substantially higher than the 42% use reported by Abbas *et al*.[7] This, likely reflects the challenges of managing critically ill children including the diagnostic uncertainty, clinical deterioration,[1,3,16] and the high frequency of culture-negative sepsis or localized infections.[17] Despite the low bloodstream culture positivity observed in the present study, empirical therapy frequently remained unchanged after 72 hours in nearly two-third of cases, suggesting persistent diagnostic uncertainty, possible over-treatment, delayed culture reporting and limited routine antimicrobial stewardship review rounds led by infectious disease specialists/ pharmacists, consistent with reports from PICUs in Germany and Brazil.[18] These findings emphasize the importance of antimicrobial stewardship and timely microbiological support to facilitate culture-guided de-escalation. Limited use of rapid diagnostic tool may also have contributed to delayed antibiotic optimization, as multiplex PCR and GeneXpert were used in only 18% of cases, similar to the findings of previous studies.[2,16] Howard *et al*. suggests that these technologies may potentially make the de-escalation of the culture-negative cases quicker and decrease the use of Watch-class antibiotics. [19]

Although, the mean duration of antibiotic exposure was relatively shorter (5 days) as compare to 6.6 days in Kumari *et al*,[1] one-third of the children still received antibiotics for >7 days, often extending beyond 14 days in HAIs. These findings are consistent with previous studies from Saudi Arabia,[3] Ethiopia,[4] and India[14.] Our study highlights that invasive device use remained a key determinant of both prolonged antibiotic exposure and HAIs. This likely reflects greater illness severity and potential AMR, underscores the need for cautious prescribing practices. These findings are consistent with previous studies,[4] reinforcing the importance of antimicrobial stewardship and strict infection control measures in PICU settings.

More than half of the children received combination therapy., and exposure to 3 or more antibiotics was associated with prolonged hospitalization, higher rates of MODS, HAIs, and mortality. Although combination therapy may be clinically justified in selected high-risk situations, excessive use of multiple agents may increase antimicrobial resistance and warrants careful monitoring to avoid unnecessary polypharmacy. These findings support previous study by Singh MP *et al.*[14], highlighting the relationship between antibiotic burden and adverse clinical outcomes.

Another notable finding was the low pathogen yield of blood culture together with a contamination rate of 16.8%, which greatly exceeded the CLSI-recommended benchmark of <3%.[20] This may reflect gaps in aseptic techniques, phlebotomy practices, or laboratory processing. Fixing these gaps may enhance diagnostic accuracy and facilitate more rational antimicrobial prescribing.

In particular, isolates of ESBL-producing *Escherichia coli* showed 100% resistance to the third-generation cephalosporin and piperacillin-tazobactam while exhibiting 100% susceptibility to the carbapenems. Similarly, *XDR Salmonella Typhi* demonstrated complete resistance to third generation cephalosporin. *MDR Acinetobacter* demonstrated 75% resistance to carbapenems, while 50% of *Enterococcus* isolates showed resistance to penicillin using CLSI criteria. These results highlight the progressive emergence of MDRO in pediatric intensive care units (PICUs) and underscores the need for continuous surveillance to guide empirical therapies and limit the emergence and spread of resistant organisms.

The predominance empirical use of Meropenem, vancomycin, piperacillin-tazobactam and colistin in the study reflects both the severity of illness and the prevalence of the MDRO. While use of these broad-spectrum agents may be clinically justified in selected patients, excessive reliance on reserve antibiotics may perpetuates resistance evolution.[3,5,21] Strengthening antimicrobial stewardship through prospective audit and feedback (PAF) led by infectious disease specialists/ pharmacists,[11,19] timely antibiotic review,[5,14] improved diagnostic capabilities,[11,21] adherence to WHO AWARE recommendations,[3,5] and strict infection prevention practices, may help optimize antibiotic use and limit antibiotic resistance.

These findings are relevant to lower- and middle-income countries (LMICs), where antibiotic usage is expected to grow by 200% by the year 2030[22] and tailored stewardship approaches could prevent 10 million deaths related to antibiotic resistance annually by the year 2050.[23,24]

This study has several limitations. Being a single-center study with a relatively small sample size may limit generalizability to other PICU in Pakistan. Inclusion of only children admitted for >72 hours might have underestimated overall antibiotic exposure. Furthermore, we did not assess illness severity scores, antibiotic appropriateness according to WHO AWaRE or IDSA guidelines, the institutional and patient-related factors underlying high culture contamination rates and excessive antibiotic use, or the LMIC-specific barriers like prescriber adherence and limited resources, which were beyond our scope. Future multicentre studies should address these factors and evaluate the impact of antimicrobial stewardship interventions on prescribing practices, resistance patterns and clinical outcomes.[25]

CONCLUSION

Antibiotic utilization in critically ill children was predominantly empirical, with limited reassessment. The observed prescribing patterns and emerging resistance trends highlights the important antimicrobial stewardship challenges and the need for improved diagnostic support, therapy reassessment and effective infection prevention to curb antimicrobial resistance.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Rubab Naz: Substantial contributions to concept, study design and acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

Hanif Kamal: Substantial contributions to study design and interpretation of data, critical review of manuscript for important intellectual content, has given final approval of the version to be published.

Anwar Ul Haque: Substantial contributions to acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

Safa Alam: Substantial contributions to acquisition, analysis and interpretation of data, critical review of manuscript, has given final approval of the version to be published.

Atika Sher: Substantial contributions to acquisition of data, manuscript drafting and reviewing it critically for important intellectual content, has given final approval of the version to be published.

Muhammad Irfan: of data, critical review of manuscript, has given final approval of the version to be published.

REFERENCES

1. Kumari A, Agarwal SC, Goyal P. Pattern of drug prescription in the pediatric intensive care unit of a tertiary care hospital with emphasis on antimicrobial utilization. J Pediatric Crit Care. 2019; 6(5): 29. DOI: https://doi.org/10.21304/2019.0605.00528
2. Ergül AB, Gökçek İ, Çelik T, Torun YA. Assessment of inappropriate antibiotic use in pediatric patients: Point-prevalence study. Turk Pediatri Ars. 2018; 53(1): 17. DOI: https://doi.org/10.5152/turkpediatriars.2018.5644
3. Kazzaz YM, AlTurki H, Aleisa L, Alahmadi B, Alfattoh N, et.al. Evaluating antimicrobial appropriateness in a tertiary care pediatric ICU in Saudi Arabia: a retrospective cohort study. Antimicrob Resist Infect Control. 2020; 9(1): 1-8. DOI: https://doi.org/10.1186/s13756-020-00842-2
4. Mohamed AA, Haftu H, Hadgu A, Seyoum D, Gebrekidan G, Ebrahim MM, *et al*. Prevalence, clinical profile and risk factors of nosocomial infection in Ayder pediatric intensive care unit, Tigray, Ethiopia. Int J Gen Med. 2022; 15: 7145-53. DOI: https://doi.org/10.2147/ijgm.s384233
5. Braykov NP, Morgan DJ, Schweizer ML, Uslan DZ, Kelesidis T, Weisenberg SA, *et al*. Assessment of empirical antibiotic therapy optimisation in six hospitals: an observational cohort study. Lancet Infect Dis. 2014; 14(12): 1220-7. DOI: https://doi.org/10.1016/s1473-3099(14)70952-1
6. Bamel VV, Shahani SR. Study of antibiotic prescription pattern in PICU of a tertiary care hospital. Int J Basic Clin Pharmacol. 2018; 7(12): 2319-24. DOI: http://dx.doi.org/10.18203/2319-2003.ijbcp20184839
7. Abbas Q, Haq AU, Kumar R, Ali SA, Hussain K, Shakoor S. Evaluation of antibiotic use in pediatric intensive care unit of a developing country. Indian J Crit Care Med. 2016; 20(5): 291-4. DOI: https://doi.org/10.4103/0972-5229.182197
8. Sharma PK, Kumar M, Sahani A, Goyal R, Aggarwal GK, Virender K, *et al*. Evaluation of antibiotics use in a tertiary care pediatric intensive care and high-dependency unit. J Pediatr Crit Care. 2020; 7(3): 131. DOI: https://doi.org/10.4103/JPCC.JPCC_58_20
9. Markham JL, Burns A, Hall M, Molloy MJ, Stephens JR, McCoy E, *et al*. Outcomes associated with initial narrow-spectrum versus broad-spectrum antibiotics in children hospitalized with urinary tract infections. J Hosp Med. 2024; 19(9): 777-86. DOI: https://doi.org/10.1002/jhm.13390 .
10. World Health Organization. (2015). Global action plan on antimicrobial resistance. World Health Organization. https://iris.who.int/handle/10665/193736
11. Fresán-Ruiz E, Izurieta-Pacheco AC, Girona-Alarcón M, de Carlos-Vicente JC, Bustinza-Arriortua A, *et al*. Antimicrobial stewardship improvement in pediatric intensive care units in Spain—what have we learned?. Children. 2022; 9(6): 902. DOI: https://doi.org/10.3390/children9060902
12. Joshi CE, Sujatha MB, Purushothaman KK. Antibiotic prescription pattern in pediatric intensive care unit in a tertiary care hospital: A cross-sectional study. National J Physiol, Pharmacy Pharmacol. 2024; 14(7):1375-9. DOI: https://doi.org/10.5455/njppp.2024.14.01007202431012024
13. Kazzaz YM, Alharbi M, Nöel KC, Quach C, Willson DF, Gilfoyle E, McNally JD, O'Donnell S, Papenburg J, Lacroix J, Fontela PS. Evaluation of antibiotic treatment decisions in pediatric intensive care units in Saudi Arabia: A national survey. J Infect Public Health. 2021; 14(9): 1254-62. DOI: https://doi.org/10.101 6/j.jiph .2021.08.021
14. Singh MP, Gaikwad NR, Keche YN, Jindal A, Dhaneria S, Gurunthalingam MP. Antimicrobial utilization in a paediatric intensive care unit in India: A step towards strengthening antimicrobial stewardship practices. PLoS One. 2024; 19(9): e0310515. DOI: https://doi.org/10.1371/journal.pone.0310515
15. Kumar R, Kumari N, Kumari S, Ansari M, Singh B. Prevalence and pattern of antibiotic usage in paediatric patients admitted in a tertiary care hospital of Bihar: An observational and cross-sectional study. Int J Pharm Sci Rev Res. 2022; 74(2): 194–9. DOI: http://dx.doi.org/10.47583/ijpsrr.2022.v74i02.031
16. Mali NB, Deshpande SP, Tullu MS, Deshmukh CT, Gogtay NJ, Thatte UM. A prospective antibacterial utilization study in pediatric intensive care unit of a tertiary referral center. Indian J Crit Care Med. 2018; 22(6): 422-6. DOI: https://doi.org/10.4103/ijccm.ijccm_365_17
17. Klingenberg C, Kornelisse RF, Buonocore G, Maier RF, Stocker M. Culture-negative early-onset neonatal sepsis-at the crossroad between efficient sepsis care and antimicrobial stewardship. Front Pediatr. 2018; 6: 285. DOI: https://doi.org/10.3389/fped.2018.00285
18. Araujo da Silva AR, Jaszkowski E, Schober T, von Both U, Meyer-Buehn M, Marques AF, et al. Patterns of antimicrobial consumption in neonatal and pediatric intensive care units in Germany and Brazil. Eur J Clin Microbiol Infect Dis. 2020; 39(2): 249-55. DOI: https://doi.org/10.1007/s10096-019-03714-9
19. Howard P, Pulcini C, Levy Hara G, West RM, Gould IM, Harbarth S, *et al*. An international cross-sectional survey of antimicrobial stewardship programmes in hospitals. J Antimicrob Chemother. 2015; 70: 1245–55. DOI: https://doi.org/10.1093/jac/dku497
20. Clinical and Laboratory Standard Institute. Principles and Procedures for Blood Cultures, 2nd ed. CLSI guideline M47. Malvern (PA): Clinical and Laboratory Standards Institute; 2022. Available from: https://clsi.org/shop/standards/m47/ISBN:978-1-68440-149-9
21. Mathew R, Sayyed H, Behera S, Maleki K, Pawar S. Evaluation of antibiotic prescribing pattern in pediatrics in a tertiary care hospital. Avicenna J Med. 2021; 11(01): 15-9. DOI: https://doi.org/10.4103/ajm.ajm_73_20
22. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, *et al*. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proceedings of the National Academy of Sciences. 2018; 115(15): E3463-70. DOI: https://doi.org/10.1073/pnas.1717295115
23. Walsh TR, Gales AC, Laxminarayan R, Dodd PC. Antimicrobial resistance: addressing a global threat to humanity. PLoS Med. 2023;20(7): e1004264. DOI: https://doi.org/10.1371/journal.pmed.1004264

24. O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. Government of the United Kingdom. 2016. Landmark report that analysed the impact of antimicrobial resistance from an economic perspective, which is the source of the highly quoted figure that antimicrobial resistance will cause. 2022; 10. DOI: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

25. Oğuz E, Bebitoğlu BT, Nuhoğlu Ç, Çağ Y, Hodzic A, Temel F, *et al*. Evaluation of antibiotic use among hospitalised patients in a paediatric department of a training hospital in Turkey. Int J Clin Pract. 2021; 75(3): e13782. DOI: https://doi.org/10.1111/ijcp.13782